IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF SOUTH CAROLINA
CHARLESTON DIVISION
CASE: 2:98-1879-23

SUZANNE Q. LITTLE, INDIVIDUALLY and as Personal Representative of the Estate of SAMUEL MARTIN LITTLE, Deceased,

Plaintiff,

-vs-

BROWN & WILLIAMS TOBACCO CORPORATION, individually and as successor by merger to THE AMERICAN TOBACCO COMPANY AND R.J. REYNOLDS TOBACCO COMPANY,

Defendants.

DEPOSITION OF: CAROLYN E. REED, M.D., Volume III

DATE: Wednesday, May 10, 2000

TIME: 8:10 a.m.

LOCATION: MUSC, Room 409
171 Ashley Avenue,
Charleston South Carolina

TAKEN BY: Attorneys for the Defendants

REPORTED BY: ROCHEL ALBERT
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It was stipulated by and between counsel for the parties that this deposition is taken pursuant to notice and that all questions as to notice are waived; that all objections, save as to the form of the question, are reserved until the time of trial; that the deposition is taken pursuant to the South Carolina Rules of Civil Procedure, for the purposes allowed therein; and that the deponent was explained her right to read and sign the deposition and reserved that right.

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CAROLYN E. REED, M.D.,

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called as a witness and having been first duly sworn, testified as follows:

D-I-R-E-C-T E-X-A-M-I-N-A-T-I-O-N

BY MS. SCHMAHL:

Q. Good morning, Dr. Reed. My name is Robin Schmahl. We actually met during the first two days of your deposition.

A. Yes.

Q. Do you understand that you are still under oath?

A. Yes.

Q. The same rules apply as to the first two days of your deposition.

A. Yes.

Q. Let me hand you what will be marked as Defendants' Exhibit Number 35.

(Defendants' Exhibit 35 was marked by the court reporter and is attached to the end of the deposition.)

Q. This is a letter that we received from plaintiff's counsel, Ness Motley, on March 21st, listing four books that you intended to rely on and noted references to those book chapters, correct?

A. Yes. I am not quite sure what you mean by "rely on" in the sense, what you asked me before was some chapters on smoking, carcinogenesis, and these were just some of the articles that exist, and I picked them out and gave them to, you are right, Ness Motley.

Q. Dr. Reed, did you understand that actually what we asked for is any materials that you yourself were relying on as the basis for any of your opinions in this case?

A. What I understood was that when I made this statement that smoking is related to lung carcinogenesis you wanted some background materials that I relied on. So I picked out some of the articles that existed in the literature regarding

this. These are book chapters. There are several references. What I tried to do is pick out the references that the book chapters had also used, so that you would have a complete set of articles. They are by no means the only articles that exist.

Q. Okay. Let me for the sake of clarity ask you, are you yourself relying on these four chapters as the basis for your opinions in this case?

A. No, not just these articles. You asked me for series of articles to back up some of what I was saying. That is my understanding. If I misunderstood, I am sorry. You asked me for a series of articles that would help back up my statement, because when you asked me, I didn't have any references with me. My understanding is that you wanted references.

These are a series of references that happened to be the easiest ones that I could put my hands on. If you wanted me to give you more references to help, I would have to go back and research all of this. This will take hours of my time.

Q. Dr. Reed, let me just ask you to answer my question. Are you relying on --

A. I am relying on some of these articles. They are not the only articles that I am relying on.

Q. I am not asking if this is the total universe of the materials that you have looked at.

A. Right.

Q. But are you relying on these four chapters?

A. Yes.

Q. Okay. My understanding from your last deposition is that the referenced footnotes in these articles, that you had not read them and that you were not --

A. That's correct.

Q. -- relying on them, and did not intend to testify about the substance of those articles?

A. Let me make myself real clear so we get this clarified. The book chapters that you have are basically a summary of the references that are listed.

Q. Okay.

A. So in order to be correct, to rely on these book chapters, you would have to go get all of these references. You would probably throw out some of the references because they probably will

not be germane, because all I could do is read the titles.

I am not going to testify that I am an expert on lung carcinogenesis, or as you asked me last time, epidemiologist. You asked me for background material for the statement that I made that lung cancer and smoking are connected.

Yes, I am relying on these book chapters to help support that statement, but you are absolutely correct that you would have to go back and get some of these references like you see on number 2, "lung cancer principles and practices." I listed references 1 through 40. It could be that 2 and 3 and 17 really aren't germane. I don't know. I would have to have somebody go get all of those references, which I would be happy to look at, but somebody is going to have to go get those references.

Q. This is what we are very much expecting to be the last day of your deposition.

A. Right.

Q. Let me just break this down. You have not read the references in Chapter 18 of the lung cancer principles and practice book; is that correct? You are not prepared?

A. Right. That is exactly correct. My understanding was that you -- when I gave you those three chapters was that if you wanted the references, somebody in your department or your office was going to get all of those references. You know, I never was instructed to go get all of those references. If you want me to, we can do that.

Q. I am in no way criticizing or saying that you should have.

A. I am simply stating that if that is what you want us to do, we are going to have to send somebody to the library to do all of that. It's not going to -- it's going to be a relatively long task. If that is what you want, then you need to clarify that today because that is going to take a tremendous amount of time.

Q. To the extent that we were going to talk about it before trial, it was to talk about it today. Would I be correct then in that sitting here today you are not prepared to talk about any of the specifics of the footnotes?

A. That's correct.

Q. Then in that case, I won't ask you any questions about the footnotes.

A. Okay.

Q. And to the extent you decide to start looking at them between now and trial, we will object to testimony on those, because we did not have the opportunity to ask you about it either today or at your earlier deposition.

A. That is up to you.

Q. Dr. Reed, since the date of your last deposition, have you discussed this case with anyone from Ness Motley?

A. I only called, I think it was this week. I called this week to simply ask whether we thought this was going to be the last day. I didn't discuss the case. I discussed the timing.

Q. Okay. Have you discussed anything with Dr. Turrisi?

A. No.

Q. Dr. Rocha Lima?

A. No.

Q. Dr. Green?

A. No.

Q. Dr. Hardly?

A. No.

Q. Anyone else?

A. No.

Q. Since March 22nd, have you reviewed any other materials with regard to this litigation in Martin Little's case?

A. No.

Q. During your last deposition after you had left we had introduced into evidence the four book chapters that are referenced in Defendants' exhibit.

A. Yes.

Q. Have you had a chance to review and read Chapter 18 of the lung cancer principles book?

A. No.

Q. When was the last time that you had reviewed that chapter?

A. Months ago.

Q. Are you prepared to discuss the conclusions reached in that chapter?

A. Not without rereading it.

Q. Sitting here today, do you know what conclusions or points contained in Chapter 18, which was Exhibit 30, you relied upon in reaching your opinion?

A. No. I would have to reread the chapter. It has been several months.

Q. Would it be fair to say that you

couldn't, sitting here today, say what conclusions or points you agreed with and what conclusions or points you disagree with?

A. Correct.

Q. On Exhibit 31, which is the epidemiology chapter from the Thoracic Surgery Book by Pierson, have you reviewed that chapter?

A. No.

Q. Are you prepared to discuss it today?

A. No.

Q. Do you know, would it be fair then that you don't know what conclusions you are relying upon?

A. Correct.

Q. You don't know what conclusions you are disagreeing with?

A. Correct. I would have to reread all of these three chapters again.

Q. Again, Chapter 19, Lung Cancer Principles and Practice?

A. Same thing.

Q. You haven't read it?

A. I have read it, but not recently.

Q. You have read it but not recently?

A. Right.

Q. Okay. You don't know what conclusions you relied upon?

A. Correct.

Q. And you don't know what you disagree on?

A. Correct.

Q. And the last one, Chapter 85?

A. Same thing.

Q. Haven't read it recently?

A. No.

Q. Don't know what you --

A. No.

Q. Doctor, let me hand you what will be marked as Defendants' Exhibit 36.

(Defendants' Exhibit 36 was marked by the court reporter and is attached to the end of the deposition.)

Q. Exhibit 36 is an article coauthored by you in 1994 entitled, "Prevalence of p53 Mutations in Patients with Squamous Cell Carcinoma of the Esophagus;" is that correct?

A. Correct.

Q. And it was published in the Journal of Thoracic and Cardio --

A. Cardiovascular Surgery.

Q. Does that appear to be a journal?

A. Yes, it is.

Q. Did you personally review the study cited in the article?

A. Yes. This was written by Christopher Gates, who is a resident in our program. He studied in the laboratory of Dr. Jonathan Bromberg. My part in this case was to supply some of the materials, the specimens that he studied. But the actual basic science was done by Dr. Gates.

Q. But would it be fair to assume that if your name is on this article you did review the end product, you did review the references?

A. Yes. Everybody that is listed as an author reviewed the article before it went out.

Q. Sitting here today, do you still stand by your article?

A. Yes.

Q. And having read the references, you are aware of medical literature that suggests that p53 mutations in lung tumors are associated with smoking, correct?

A. Correct.

Q. Directing your attention to the first paragraph of page 148. Your article concludes that coastal South Carolina has one of the highest rates

of squamous cell esophageal cancer in the world; is that correct?

A. That's correct.

Q. More than four times the global average?

A. Correct.

Q. Are you aware of any medical literature discussing the higher incidence of lung cancer in coastal South Carolina?

A. No.

Q. Going on to the next paragraph on page 148 of Exhibit 36, your article acknowledges that the following substances have been most frequently implicated in the development of esophageal cancer; tobacco, correct?

A. Yes.

Q. Alcohol?

A. Yes.

Q. Opiates?

A. Yes.

Q. Aflatoxins?

A. Yes.

Q. Caustic agents?

A. Right. These are world environmental exposures. What I mean by that is that, for example, caustic agents is probably worldwide.

Aflatoxin is probably more limited to certain parts of the world. There's an esophageal cancer belt across the world, and there are probably different agents in different parts of the belt that have something to do with esophageal cancer. Tobacco and alcohol are well-known risk factors for squamous cell cancer of the esophagus.

Let me just say that since this article has been published, we do not have as high a rate of esophageal cancer in South Carolina. We, like everybody else in the state, is seeing a rise in adenocarcinoma, and that has now superseded in our tumor registries squamous cell carcinoma, just for the record.

Q. I am curious which opiates have been implicated in the development of esophageal cancer.

A. These are probably related to opiates -- squamous cell carcinoma of the esophagus is very well-known in the belt across northern China where they smoke all kinds of weird substances with some opiates. Like, for example, tea leaves and things like this have some substances in them that have been purported to be associated with cancer.

And it goes back in China to the fact that the areas that have a large number of squamous

cell carcinoma, they have a number of practices that are relatively strange, and they drink hot tea and they smoke what is called beetle nuts and things like that. And some of those substances are probably involved with lung cancer.

I don't know of any direct work that has looked at, for example, taking mice and giving them these substances and have them develop cancer. Most of this listed right here, this sentence that you just stated, is related to epidemiologic studies, putting together unusual substances with the fact that there is this incredible hot spot across -- around the Caspian, across China. In the United States. It's Washington, D.C. and the coastal Lowcountry of South Carolina. That is for squamous cell.

Q. But your understanding is that, at least for squamous cell cancer, that those are inhaled opiates, beetle nuts, opium, things of that nature?

A. I would guess so, yes. I am just talking about -- this opiate is directly related I think to the belt in China, not the United States.

Q. Would you consider marijuana to be an opiate?

A. Uh-huh, yes.

Q. Would you consider cocaine to be an opiate?

A. Yes.

Q. Continuing at the top of the second column on page 148, your article suggests that there may also be an underlying genetic predisposition for esophageal cancer in some cases; is that correct?

A. Yes, very unusual genetic syndrome. Tylosis is extremely unusual and so is Li-Fraumeni syndrome.

Q. If you turn, please, to page 149 under the results section.

A. Yes.

Q. Your team had conducted p53 testing on 15 different squamous cell samples, correct?

A. Right.

Q. According to your article, 10 of the specimens exhibited at least one p53 mutation?

A. Correct.

Q. Then two-thirds of the squamous cell cancers that your team examined showed genetic mutations?

A. Showed point mutations, yes, that are in the genes, which can be either -- that doesn't mean

it necessarily is inherited. That means that there's been a mutation. There could have been an environmental cause. It could have been in the genes. Who knows.

But, yes, you are correct that about -- and that actually goes along with the literature, about 50 to 60 percent of squamous cell cancer of the esophagus has -- this was done with Polymerase chain reaction. So this is quite specific.

Q. But this was specifically testing for p53?

A. P53, yes.

Q. Turning your attention to the second full paragraph in the second column, the second full paragraph in the right column on page 150. Your article states that a great deal of interest has been generated in whether, quote, specific mutations can implicate the etiology of a tumor, correct?

A. Where are you reading?

Q. Sorry. Page 150.

A. 150. I'm sorry.

Q. Right-hand column.

A. Got you.

Q. Second full paragraph.

A. Right.

Q. Would you like for the court reporter to reread the question?

A. Do you mind if I just reread this for a moment?

Q. No.

(The record was read by the reporter.)

Q. And you go on to note that all 15 of the patients from whom the squamous samples were taken had a significant history of tobacco use?

A. Correct.

Q. What do you consider a significant history?

A. Probably greater than 30 or 40 packs a year history.

Q. And then later on in that paragraph you go on to cite a study by Field, which is this study footnoted at reference eight, which found 78 percent of smokers that they tested had p53 mutations compared to 14 percent of nonsmokers, correct?

A. That is what it states, yes.

Q. So your team found 67 percent, roughly two-thirds, with squamous cells had p53 mutations, and the study cited here had about 78 percent,

correct?

A. Correct.

Q. Is that consistent with the medical literature on the prevalence of p53 mutations?

A. In squamous cell cancer, yes, of the esophagus.

Q. Just backing up a bit to the discussion section on page 149. It's in the right-hand column. Your article states that squamous cell carcinoma -- sorry, let me be more specific -- that squamous cell esophageal cancer is, quote, of particular interest because epidemiological data suggests many environmental exposures that may be associated with an increased risk of its formation, correct?

A. Correct.

Q. Have we already discussed this sort of environmental and genetic?

A. Right. That goes along with the fact that epidemiologically the hot spots are clustered. So what happened is these people went to these hot spots and looked at various social and environmental factors that might be connected to squamous cell carcinoma.

Again, it goes back to the hot tea and

the beverages, and this squamous cell carcinoma is extremely rampant, if you will, in South Africa and parts of Africa where it may be related to lack of minerals, certain grains, et cetera.

The problem with this whole thing is that what was hoped was that because there are certain cluster hot spots over the world, that when epidemiologists visited these hot spots there would be one agent that was sort of common among this group. Unfortunately that is not what they found. They found what is stated here, that there may be a variety of environmental factors that are connected with squamous cell carcinoma of the esophagus.

Q. And those are what we have already discussed, the opiates, the tobacco, the hot tea, beetle nuts?

A. All that sort of thing. Lack of minerals, it could be selenium and zinc. It's actually a pretty long list. I would have to go back to look to make sure. The items that we have stated have all been stated before as possible environmental factors that may increase a person's risk for squamous cell carcinoma of the esophagus.

Q. And that would be social behaviors like the tea drinking, correct, as being one --

A. For example, yes. In China they drink a lot of hot tea, so one of the questions is are they using a substance in their hot tea that is very different from the English tea, et cetera, things like that. If you are in a country that is very poor and the soil is lacking X, Y, Z minerals, is there any possibility that could have anything to do with it?

The problem with all of this that we are talking about is whether there's a true cause and effect rather than a simple linkage of here's an item and here's something, are they linked. It's very difficult to prove.

Q. Right.

A. I will give you another example. It's been stated that perhaps moonshine in South Carolina has something to do with squamous cell carcinoma of the esophagus because of the high incidence of squamous cell carcinoma in the Lowcountry occurs among black males, particularly alcoholics. And many of these black male alcoholics fix their own alcohol. And so there's been a suggestion.

But if you go back and read some of this literature it's a very loose connection. It's not

that we gave a rat moonshine and they developed squamous cell carcinoma.

Q. Right.

A. So it's -- a lot of epidemiological study is very soft in that regard. That is all that I mean. It's very hard to say. You really can't make the statement that this causes the cancer. All you can look at is associations.

Q. Right.

A. And these that you have listed and we have talked about so far are associations.

Q. Because in all of these cases, as you said, you can't make a rat drink some hot tea and see if it has squamous cell cancer?

A. Right.

Q. Or have it smoke a little beetle nut to see what happens?

A. The problem with all of this is what is probably going on is a lot -- it's a multifactorial -- carcinogenesis is a multifactorial process. So you have -- you might have an underlying genetic instability, you might have an underlying genetic process that needs to be triggered and that trigger could be a variety of environmental projects. And we are finding that

more and more now. There's just thousands of mutations that are involved in the development of cancer probably.

Q. And diet may have an effect on it?

A. Diet may. It may have an effect. For example, if you are predisposed to colon polyps, can you make it better by eating a diet with more fiber? Well, you know, an article just came out that disputes that, even though that has been the association and why everybody has been doing it. That is what I mean by some of the weak links in epidemiologic studies.

Q. And then heredity may have some factor in the development of cancer?

A. Everybody in this room has oncogenes that are existing in their body right now that can be turned on or off. The question is, what turns them on and what turns them off? You have the genes for cancer right now in your body, but you have either repressor genes or growth factors that have been turned on or off, depending on whether they are repressors or growth factors.

So we all have the genes for cancer. We know that now. The question is, what are the trigger factors that turn some of these genes on

and off? And if they are turned on, what is their mechanism so we can plot that mechanism?

Q. And with respect to the things that turn them on, that would turn on the oncogenes, that is part of that whole multifactorial environmental exposure, heredity?

A. There are probably a variety of -- there most certainly are a variety of agents that can do that.

Q. And that would be true for lung cancer as well as esophageal cancer; is that correct?

A. Yes. We believe that all cancers are like that. The problem is there are going to be certain triggers that are more associated with some cancers than others. For example, p53 mutation is very widespread in solid tumors. So it probably is one of the early mutations that can occur in a number of cancers. But when and where and what it gets triggered, it is probably one of the least specific mutations because it's so widespread.

It would be nice if, gee, squamous cell carcinoma is the only cancer that p53 was a mutation in, because then it would give more impetus to do something with p53. It so happens that p53, because it's a general tumor suppressor

gene, is involved in a lot of different cancers.

Q. Okay. In your opinion, is there a high prevalence of p53 mutation of the squamous cells irrespective of where the tumor is located?

A. I would have to really look at that. I don't have it on my fingertips the various list of cancers and what articles.

Another problem with this whole research is that the reason we got a high number in this article of p53 mutations is if you notice that we looked at point mutations with Polymerase chain reaction. Most p53 mutations are now being looked at with immunochemistry, i.e. antibodies. Some of those antibodies only react with -- if you read the article you will see that there are actually several different mutations.

Q. Yes.

A. So it could be an exon 9 or an exon whatever. Some of those monoclonal antibodies only bind with one mutation rather than some of the others. So the reports are all over the map. If you want to read about p53 mutation, you can pick up a book that says p53 mutation, for example, in lung cancer ranges from 30 to 60 percent. That is quite a range, and probably has to do with the

methods of detecting p53 mutation. If you want my opinion, p53 mutation is quite widespread, but I am not prepared to give you for each cancer an exact.

Q. So there's more than one way to check for p53 mutations. Is it the immunohistochemical stain?

A. There's immunochemical stains using monoclonal antibodies against various things. The Polymerase chain reaction that is stated is very time-consuming. And when you are looking at the gene sequencing and looking at all the point mutations, you are going to pick up more mutations than you are with monoclonal antibodies.

Q. In your opinion then, this chain reaction is a more sensitive test than doing --

A. Yes.

Q. You recognize genetic testing for p53 besides the immunochemical testing, correct?

A. Say that again.

Q. Do you acknowledge the validity of p53 testing besides simply immunochemical staining?

A. I am just telling you there's a variety of methods to look for p53 mutations, which I am certainly not an expert in. Let me just say that up front. What you will see in the methods section

is that these tumor biopsy specimens were either grown in tissue culture or they were cryoprecipitated to get the raw RNA and DNA of the specimens.

Most people that are dealing with p53 mutations today are taking -- for example, the tumor specimen that comes out of the body, they are taking the slide that they looked at under the microscope and they are simply running a, if you will, an antibody test or immunochemical test, if you will, on that slide. That is very different from taking the tumor tissue itself and looking at the RNA from the tumor tissue.

And what I am saying here is that I believe you taking the RNA or DNA and taking it directly from the tumor is going to be much more -- probably more precise than simply running an antibody stain. So there's just a variety of ways to look at it. And that is the reason when you read the literature it says 30 to 60 percent of these tumors may have p53 mutations. It's not very precise. The reason it's not very precise is that not everybody is using the same test.

Q. Okay. In your opinion are p53 mutations caused by tobacco smoke? Is that the conclusion

that you have drawn?

A. My conclusion or my -- it's probably better to say supposition -- is that tobacco smoke is probably one of those factors that can result in a point mutation that results in a mutant p53.

Q. Let me ask it this way. If a cancer patient was positive for p53 mutation, and you knew that that patient was a smoker, could you opine with a reasonable degree of medical certainty that the mutation was caused by tobacco smoke?

A. Not necessarily. There can be all kinds of reasons. We just said there's a number of environmental causes for -- you cannot -- you can't connect the two because somebody smokes and they have a cancer and they have a p53 mutation. I don't think that you can say he is a smoker, therefore, his p53 mutation came from smoking.

Q. Okay.

MS. SCHMAHL: Actually, would you mind if we take a break?

(A break was taken.)

BY MS. SCHMAHL:

Q. Jerry, I just wanted to put on the record a significant portion of the remainder of our portion has to do with those specific discussions

of the four book chapters that were references, reliance materials in Defendants' Exhibit 35.

My understanding from the testimony is that Dr. Reed has not read them recently, is not prepared to discuss them in detail, is not certain what she agrees with or what she disagrees with.

Do you have any different understanding of her testimony?

MR. EVANS: I am not going to discuss that on the record. You are welcome to repeat your questions. I think you have covered that with Dr. Reed, and I think that testimony is clear.

MS. SCHMAHL: Well, because my understanding is that this is not an area that Dr. Reed is prepared to go into today, I am not going to ask my series of questions on the four book chapters referenced in Defendants' Exhibit 35, and just for the record, we will object if it comes up at trial to testimony on this subject, because we were not given the opportunity to do a full examination today or during the earlier deposition on these four book chapters.

A. You didn't ask me to read them. I will be happy to do that. And if you want to come back and have me do that, I will be happy to do that,

but nobody asked me to do that.

Q. Right. That is just a lawyer thing.

(Defendants' Exhibit 37 was marked by the court reporter and is attached to the end of the deposition.)

Q. Dr. Reed, I am going to hand you what will be marked as Defendants' Exhibit 37. This is an article entitled "Bronchioloalveolar Carcinoma" by John Barkley and Mark Green, correct?

A. Yes.

Q. And it was published in the --

A. Journal of Clinical Oncology, 1996.

Q. And is that a peer review journal?

A. Yes, I believe so. It's a medical journal.

Q. Dr. Mark Green, the coauthor of that, he is the head of the Hollings Cancer Center here at MUSC; is that correct?

A. Correct.

Q. I just want to go through this article with you a little bit. First, let me ask you about some statements that appear in the summary which is at the top of the left-hand column on page 2377. Is that called the abstract, that bolded portion on the top --

A. Right.

Q. -- of 2377? Starting with the second sentence in the summary under "results," it says, quote, patients with BAC tend to be younger at diagnosis. Would you agree with that statement?

A. I would have to do the research because I agree with the second, they are more likely to be females. My experience is they are all over the map. I will accept what he said if he has reviewed the article. I would have to go back and look at references. That is not a common thing to my knowledge, but the second is. They are more likely to be female.

Q. How about the third, less likely to be cigarette smokers?

A. Correct.

Q. If you would look, please, at the table that is on page 2379 of Exhibit 37.

A. 2379?

Q. Yes, ma'am.

A. Okay.

Q. There is a little table at the top of the left-hand column, "Table I. Diagnostic Criteria for BAC." Would you agree that no evidence of extra thoracic adenocarcinoma is one of the diagnostic

criteria for BAC?

A. Yes.

Q. Would you agree that absence of a central bronchogenic source is a diagnostic criteria?

A. Yes.

Q. Would you agree that peripheral parenchymal location is a diagnostic criteria?

A. Yes.

Q. Would you agree that no distortion of the pulmonary interstitium is a diagnostic criteria?

A. Yes.

Q. Would you agree that neoplastic cells growing along alveolar septae is a diagnostic criteria?

A. Yes.

Q. Would you add anything for the diagnostic criteria for BAC?

A. Not right off the top of my head.

Q. If you think of anything during the course of the deposition, would you let me know?

A. Sure.

Q. Also on page 2379 of Exhibit 37, the last full paragraph in the left-hand column, Dr. Green has a discussion about the literature showing an apparently inconsistent finding of an increased

odds ratio for the development of BAC following quitting smoking.

A. Tell me where you are.

Q. It is the last full paragraph in the left-hand column on page 2379.

A. I got you. I found it. I am reading it.

Q. Just tell me whenever you are done.

A. Yes. Go ahead.

Q. Would you agree that there are some increased odds ratio for developing BAC after quitting smoking?

A. I have no idea.

Q. It goes on in the last sentence of the last full paragraph in the left-hand column, it says that more work to evaluate cigarette smoking as a possible etiologic agent in BAC needs to be performed. Would you agree with that statement?

A. Yes.

Q. And the next statement, the next sentence which is the beginning of the following paragraph notes that a vital etiology for BAC has also been postulated. Would you agree with that statement?

A. I don't know anything about that.

Q. I am referring to the first full paragraph on 2379. It's actually two paragraphs

up. Dr. Green notes that BAC may arise in lung parenchyma damaged by prior tuberculosis, pulmonary infection or abscesses and/or abscesses and pulmonary fibrosis of any cause. Would you agree with that statement?

A. Yes.

Q. Moving on to page 2380. Sorry. If you could go back to 2379. It would be the second full paragraph in the left-hand column of 2379.

The impact of cigarette smoking on induction of BAC is somewhat controversial. Would you agree with that statement?

A. Yes.

Q. On page 2380 of Exhibit 37, Dr. Green discusses molecular biology. He has got a section there. Do you see that?

A. Uh-huh.

Q. Under that molecular biology section there's a statement that the role of oncogenes and tumor-suppressor genes in lung cancers are receiving much attention. Would you agree with that statement?

A. True of all cancers today, correct.

Q. They go on to say that the prevalence of activated or overexpressed oncogenes or of mutated

Q. The next sentence after that states, "Prior pulmonary parenchymal damage, various occupational exposures, tobacco smoking and retroviral infections have all been implicated."

A. They have all been suggested as possible etiologic agents.

Q. Would you agree with that as far as it relates to BAC? Do you have any reason to disagree with that?

A. No reason to disagree with the statement.

Q. If I can get you, please, just to turn back to page 2379 of Exhibit 37. There's a section in the right-hand column of that that is entitled "Histopathology." That first sentence under the title "Histopathology" states that, "The histological classification of NSCLC can be difficult." Would you agree with that statement?

A. Not particularly, no. I am not sure. I think you are reading this out of -- I think what the statement means -- if you read the whole statement it says the histological classification of non-small cell lung cancer can be difficult with the subclassification of adenocarcinoma into acinar papillary mucus secreting and bronchioloalveolar even more difficult.

I don't even know what that first sentence means because most of the final pathology in non-small cell lung cancer is adequately classified, whether it's adenocarcinoma, large cell or squamous cell. And if it's not, then they do special staining to make it more adequate.

I am not sure I necessarily agree with that statement. There is nothing stating here, for example, in "X" number of cases or whatever. That is a pretty general statement. I am a little surprised that it's been made.

Q. So you do not agree that --

A. The histological classification of non-small cell is difficult?

Q. Right.

A. It can be difficult, but is it usually difficult? No. I don't know how you are interpreting -- I don't want me to read what you are saying. You have got histological classification can be difficult. In some case it can be difficult. But in general is it difficult? No.

Q. Would you agree that there is a degree of variability in classifying of non-small cell lung cancers?

A. Sure.

Q. Would you agree that it was the case in this case, one pathologist looks at the slide and says that it's squamous, another pathologist looks at the slide and says that it's large cell lung cancer?

A. Large cell lung cancer is a wastebasket term. Most large cell lung cancers are either very undifferentiated squamous cells or special staining adenocarcinomas.

Q. Okay.

A. So those of us that use the term "large cell carcinoma" understand that when you get to large cell carcinoma, it's a very malignant cancer and it's usually undifferentiated. So it's very hard by special studies sometimes to clarify whether it was the squamous line or the adenocarcinoma line.

Most of us feel that large cell carcinoma is probably more likely a subvariant of adenocarcinoma rather than the squamous, but it can work either way. That is why we have large cell carcinoma. Frequently you get a whole battery of special stains to see which side it's on, whether it goes towards squamous or towards adenocarcinoma.

The important point is that large cell is not a small cell. It's a non-small cell lung cancer.

Q. And that for purposes of treatment is really what's important?

A. That's correct. The most important thing for treatment is are you dealing with a small cell or a non-small cell.

Q. Would you agree that the more experienced that the pathologist is, their ability to identify BAC would improve?

A. I would definitely agree that a pathologist that is a lung cancer specialist pathologist will be better at diagnosing BAC than not.

Again, BAC comes in a variety of forms. And when it's in the form that it's growing along this septum, like you have your criteria up here, neoplastic cells growing along alveolar spaces, that is very classic of bronchioloalveolar carcinoma.

So of all the diagnostic criteria that you asked me to look at, that is the most diagnostic. In its best form bronchioloalveolar carcinoma has a very classic look to it on light microscopy.

Q. We have discussed from your article a number of factors that are at least statistically associated with lung cancer, tobacco, correct? Alcohol, yes?

A. With lung cancer?

Q. No.

A. With esophageal cancer?

Q. That is associated with esophageal cancer?

A. Squamous cell carcinoma. You have to be careful there because there are two major types of cancer in the esophagus. Of squamous cell carcinoma of the esophagus, tobacco, alcohol, previous head and neck tylosis, caustic agents, et cetera.

Q. In your opinion then would alcohol not be a risk factor for lung cancer?

A. To my knowledge, it is not a factor.

Q. Could you cite me to any medical literature or anything that would --

A. If you go back, for example, and look at those chapters, alcohol, to my knowledge -- again, I would have to review them again -- is not right up there as one of the causal factors.

Q. Are you aware of any medical

literature -- have you done a study of the medical literature to determine one way or another whether alcohol is a risk factor for lung cancer?

A. I would have to go back and look at the literature. It's not common. It's not on the tip of your tongue when you are talking about is it related like squamous cell carcinoma of the esophagus. If you had said adenocarcinoma of the esophagus I wouldn't have named alcohol. If you say lung cancer to me, I wouldn't have named alcohol.

Q. Okay. We had already discussed during your previous depositions marijuana. Since the time of your previous deposition, have you done any Med-line searches or any further research on any association?

A. No.

Q. Are you aware of medical literature that discusses caustic agents as a risk factor for lung cancer?

A. What is your definition of caustic agent?

Q. Well --

A. Caustic agents are usually drunk. So you are talking about caustic agents drinking lye, acid, therefore, that is why you talk about caustic

agents in the G.I. tract. It's hard to get caustic agents into your lungs.

So it depends on what your definition is. To me when you say caustic agent what we are talking about in medical literature is like lye or -- let me go back to say the best way to explain that is it's listed as, for example, a causative agent of esophageal cancer. That comes from small kids that got in and drank lye or acid or something like that. It's usually lye. And then 40 years later developed cancer of the esophagus.

We know that those kids that drink that or have caustic lye ingestion are at an increased risk in the future to have squamous cell carcinoma. So that would not be a cause of lung cancer because when you drink you don't get lye into your lungs.

Q. Are caustic agents a risk factor for esophageal cancer because it causes scarring?

A. Yes. It's probably related to the scarring, and they get squamous cell cancer, not adenocarcinoma.

Q. In your opinion, is indoor Radon exposure a risk factor for lung cancer?

A. It has been purported to be. I am not an expert in epidemiology or Radon exposure. It is

uniformly listed when you get an article about the epidemiology of lung cancer as one of those factors that has been associated with a higher risk.

Q. Is it correct that another risk factor that is uniformly listed is occupational exposures?

A. Secondhand smoking, asbestos.

Q. Nickel?

A. Coal miners, nickel, yes.

Q. Vinyl chloride?

A. Vinyl chloride.

Q. Are you aware of the medical literature that discusses a high animal fat diet as being a risk factor for lung cancer?

A. No. No, I am not. I know diet has been purported to be connected with everything. I am not really -- I have not read a lot about dietary factors per se relating to lung cancer. I am sure there have been some studies that looked at that, but diet is a very broad -- it's very hard to link diet unless you are specific to various cancers. It's more related to G.I. cancers.

Q. Would it be correct to say that there is literature out there, but you yourself have not recently reviewed them or done --

A. I guess I would have to say that

higher risk.

Q. Would you agree that the number of cigarettes that a person had smoked over their lifetime, their pack per year history, is a risk factor in lung cancer?

A. Yes.

Q. The more you smoke, the higher your risk of cancer would be?

A. The amount of cigarette smoking and the age that you started smoking is considered a risk factor. Having said that, half of all patients today that get cancer are former smokers. They are smokers that have quit, which most people don't understand. It's relatively interesting. It certainly is true that -- I think that may play a role in the age you start and then your exposure.

The problem is that if half of the population that are going to get lung cancer are former smokers, that means that the initial, if you will, damage that somehow turns an oncogene on or off and why do they wait so long to do it is still relatively unknown.

I think that the age may play just as important of a role as the amount of cigarette smoking. I think a lot more work needs to go into

that. But you're correct. That is listed -- if you ask a patient, the higher their pack per year history is, then you can say, why does this person who quit 14 years ago and only had a 20 pack year history is in my office with lung cancer, and this guy over here has smoked three packs per day from age 5 to 90 and he doesn't have lung cancer.

It's really tough, but if you ask what the common risk factors are, it's the age they started smoking, the amount of cigarettes per day that they smoked. Is a half a pack more damaging than a pack? I don't think we know that. But the span of time they smoked is probably important because it increases their exposure over time to whatever the factor is.

Q. I believe that you have noted in your medical records that Mr. Little smoked one pack per day for 20 years?

A. Correct.

Q. Do you have any knowledge as to whether he smoked filtered or unfiltered?

A. No.

Q. Do you have any knowledge as to whether he smoked a high tar or low tar brand?

A. No.

Q. Regular or menthol?

A. No.

Q. Do you have any knowledge as to whether Mr. Little was exposed to Radon?

A. No.

Q. Did you ask him?

A. No.

Q. Do you have any knowledge as far as the fat content of Mr. Little's diet?

A. No.

Q. Is that a question that you would have asked him?

A. No.

Q. Whether Mr. Little had relatives with cancer?

A. I didn't ask him that. Usually at some point either the internist or the medical resident probably asked him for a family history. I didn't.

Q. Was that information that you would have reviewed?

A. It may be. We have to go back to the exhibit that I think it was either Glady Brooks. PA, the physician assistant that worked him up. There was a section in that original history and physical that is usually listed as family history.

I don't remember whether she filled that in or not. Unfortunately it's not one of the common things that interns do.

Q. Do you have any knowledge as to whether Mr. Little ever had pneumonia or any other pulmonary infection?

A. I don't recall. I would have to go back and look at the record.

Q. If the records that you authored don't reflect any history of a pulmonary infection --

A. Unless he had some minor respiratory tract infection that he went to his internist for, I wouldn't have known that. It would have been what got him to the doctor. A lot of people present with lung cancer and they go through a month of back and forth on antibiotics and that could be part of the history. I don't recall if that was his history. I recall that he was sent to me with this abnormality on an X-ray, boom, here, take care of it.

Q. Do you generally ask questions as far as prior pulmonary infection?

A. Yes. I usually do, and it's related to the fact that they are going to have surgery. Their prior pulmonary history is important to what

their pulmonary function is going to be and their ability to get through the operation. I am very interested in whether they have asthma or CPLD or constant respiratory tract infections, previous pulmonary surgery, things like that.

Q. Do you generally ask a patient have you had pneumonia?

A. Yes.

Q. Where would that information be reflected in your medical records?

A. It should have been reflected -- and if it was an important part of the history, and I thought it was going to be important on the surgical history, it would either have been in my note or it would have been in the intern's or PA's note.

Q. Dr. Reed, can you rule out that Mr. Little's cancer may have been caused by occupational exposures to carcinogens?

A. You can't rule it out because I don't know what his exposure was.

Q. Could you rule out that his cancer was caused by indoor Radon?

A. Only, I don't know if he had it in his house.

Q. History of having marijuana use?

A. Again, I don't know any connection between marijuana and lung cancer, so I can't speak to that.

Q. And you don't have any knowledge as far as what his marijuana use is, correct?

A. I did not ask him about that.

Q. Or cocaine use?

A. No.

Q. Could you rule out that his cancer was caused by genetic predisposition?

A. No, I didn't look at his genes.

Q. Doctor, would you know Mr. Little's relative risk of developing lung cancer from indoor Radon? Would that be a sort of calculation that you could do?

A. No. I can't remember -- I will be honest with you -- in 15 years of asking anybody about their Radon exposure, if that helps.

Q. But that is as far as you don't know about his Radon exposure. If you did know about his Radon exposure, would you be able to tell me what his relative risk for developing lung cancer would be?

A. I have no idea.

Q. Would this be true if you did know about his occupational exposure? Would you be able to then tell me what his relative risk of developing lung cancer from those exposures was?

A. The only way to do that would be, let's say he was a uranium miner. I think if you have something like that you can go back to the literature, because epidemiological studies have been done. You could give a broad he is 40 times higher than whatever. You are 40 times higher than the general population that you are going to have adenocarcinoma, something like that.

I think that would be very difficult to do because you are not going to be able, since we don't know what all the environmental -- you would have to know the length of exposure and the time. I think you are talking about a very nebulous situation here. I wouldn't be able to take any of the things that you said and say what is the relative risk.

Q. That's not what thoracic surgeons do, correct?

A. Right. It's very difficult information to get ahold of because everybody has different exposures. That is why the only studies that have

been done like that are very specific, uranium mine workers, et cetera. You are talking about somebody who is like you and me out in the world. So that is a very difficult thing, unless -- again, even asbestosis, which we know is related to mesothelioma, if you worked all your life in asbestosis, for me to even tell you what your increased risk is compared to somebody who lives and just happens to be in a house with asbestos I think would be difficult.

Q. And that is the sort of thing that epidemiologists with a supercomputer --

A. I am trying to say even then you are going to get -- like you have already used the term "increased risk." What does increased risk mean? Is it four times, five times, six times? I think -- all that study that they do, epidemiologists' data, a lot of it is, in my opinion, soft because, again, you are looking at links and not let's give the rat the poison and you get the data. That is a very different science from a cause and effect, put two chemicals together and get the result or take a gene and break it down, et cetera. You are talking about associations.

So you can say that if you study this population and they happen to have more association, you know, to make the statement that this is a risk factor in my mind is a little soft science.

Q. Would it be fair then you sitting here today that it would be outside your area of expertise to offer a number of what Mr. Little's relative risk of developing lung cancer from smoking from a 20 year, 20 year pack history of low tar cigarettes?

A. Right. The only thing that I can testify to this whole thing is; A, as I said before when you asked me, I am not an epidemiologist, nor will I testify that I am an expert in epidemiology. If you ask me did this man have risk factors that could lead to lung cancer, my answer is going to be the same as I answered months ago. He is a smoker and smokers are increased risks to get lung cancer.

So is that what caused his lung cancer? Again, it's a risk. He has an associated factor with known increased lung cancer. What is his specific risk? I don't think anybody can tell you that.

Q. Is it fair to say then in light of that

statement that you could not testify with a reasonable degree of medical certainty that smoking alone was the cause of Mr. Little's lung cancer?

A. Smoking alone?

Q. Yes. Or that smoking was indeed the cause of Mr. Little's lung cancer.

A. What I would testify to is that smoking is a risk factor of lung cancer. He was a former smoker. He was therefore at increased risk compared to the nonsmoker of getting lung cancer. Was it the exact cause of his lung cancer? No, I can't say that. I can't say that.

You know, unless I take a gun and shoot you, I know that is what caused the hole. No, you can't do that. Again, this is -- you are back to -- I just -- if you ask me do I know that his smoking caused his lung cancer, no. Is it an increased risk that led to it? Yes, I think it is.

Q. Doctor, you have discussed a little bit about the difference between epidemiology and animal studies where you give the rat the substance and the rat then develops a term.

A. Right.

Q. Are you aware of any medical studies or published literature where they administered

cigarette smoke to a rat, inhaled and they developed lung cancer?

A. Yes. Beagles. It occurred in dogs actually. The study was done a long time ago. There have also been some studies in San Diego by Dr. John Benfield's group that looked at some of the carcinogens in cigarettes and what they caused in mice. I don't know if he used mice or rats. He has a model. But there was actually -- it was a long time ago -- a model. It was actually beagle puppies.

Q. Your file, I believe, showed that you received copies of the CVs for at least one of defendants' expert witnesses. And you have received those from plaintiff's counsel. Do you know why Ness Motley sent you those?

A. Can you tell me what I received?

Q. I believe you received CV in expert disclosure for Dr. Sanford Barsky.

A. Who is he? Can you tell me who he is so that will ring a bell?

Q. He is one of the defendants' expert witnesses in this case.

A. What does he do? That is what I am asking. What is his specialty?

Q. He is a pathologist.

A. A pathologist?

Q. Yes. Do you recall having received any expert disclosures?

A. Yes. That is why I am asking. I think it was a pathology report. So it must have been Dr. Barsky because that name is also ringing some bell in the back of my head. That is why I was asking what he does. I did receive an expert testimony, a copy of somebody who had rendered an opinion regarding pathology.

Q. Okay.

A. It's been a long time since I read it, but I do remember getting it, yes.

Q. What were you asked to do with that information? Were you asked just to review it?

A. As I remember, it was sent FYI. I was not asked to review it in preparation for testimony or anything like that.

Q. Other than the one that you believe was on pathology, did you receive any other disclosures or CVs for your review?

A. I don't remember that I did, but I do remember the pathology one.

Q. Have you ever heard of Sanford Barsky of

UCLA?

A. No.

Q. Can we just take a quick break? I think we are about done.

(A break was taken.)

MS. SCHMAHL: That is all that we have.

MR. EVANS: Any questions?

MS. HUGHES: No.

MR. EVANS: I have no questions at this time.

MS. SCHMAHL: Doctor, thank you.

(Ending time: 9:30 a.m.)

CERTIFICATION OF REPORTER

I, Rochel Albert, Certified Court Reporter and Notary Public in and for the State of South Carolina do hereby certify that CAROLYN REED, M.D. was duly sworn by me to testify to the truth, and that the above deposition Pages 87 through 142, inclusive, was recorded stenographically by me and transcribed through computer-aided transcription by me to the best of my ability.

I further certify that the foregoing transcript is a true and correct transcript of the testimony given by the said witness at the time and place specified.

I further certify that I am neither attorney or counsel for nor related to or employed by any of the parties to the action in which this deposition is taken, or financially interested in this action

IN WITNESS WHEREOF, I have set my hand and seal this 24th day of May, 2000.

Rochel Albert

ROCHEL ALBERT
CERTIFIED SHORTHAND REPORTER
NOTARY PUBLIC FOR SOUTH CAROLINA
MY COMMISSION EXPIRES: JULY 2008

CASE: LITTLE V. BROWN & WILLIAMSON, ET AL

WITNESS: CAROLYN REED, M.D. Vol III

SIGNATURE OF DEPONENT

I have read the entire deposition. To the best of my knowledge it contains a true and accurate transcript of the proceedings had at the time and place herein mentioned. Any corrections that I have are contained and described on the following correction sheet.

Signed this the _____ day of _____, 2000.

_____

CAROLYN REED, M.D.

CASE: LITTLE V. BROWN & WILLIAMSON, ET AL.
WITNESS: CAROLYN REED, M.D. Vol III

CORRECTION SHEET

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EXHIBITS